UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/515,513	02/29/00	LI W	0942.4870001

HM22/0223

Robert W. Esmond
Sterne Kessler Goldstein & Fox PLLC
Suite 600
1100 New York Avenue NW
Washington DC 20005-3934

EXAMINER	
TAYLOR, J	
ART UNIT	**PAPER NUMBER**
1655	11

DATE MAILED: 02/23/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/515,513	Applicant(s) LI ET AL.	
	Examiner Janell Taylor Cleveland	Art Unit 1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 January 2001* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *33-104* is/are pending in the application.

4a) Of the above claim(s) *64-104* is/are withdrawn from consideration.

5)☒ Claim(s) *47-63* is/are allowed.

6)☒ Claim(s) *33-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15)☐ Notice of References Cited (PTO-892)
16)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18)☐ Interview Summary (PTO-413) Paper No(s). _____ .
19)☐ Notice of Informal Patent Application (PTO-152)
20)☐ Other: .

DETAILED ACTION

The following Office Action is based on the Amendment and Reply filed by Applicant on 1/20/2001. The Restriction is based on the claims as amended. Since Applicant elected by phone, following the Restriction is a detailed Office Action pertaining to the elected group (Group I). Following the Office Action is a Response to Arguments section. Any rejection not reiterated below is hereby withdrawn. This action is made **FINAL**.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 33-63, drawn to a method for synthesizing one or more cDNA molecules, classified in class 435, subclass 6.

   II. Claims 64-104, drawn to a method for producing full length cDNA and kits pertaining thereto, classified in class 435, subclass 6.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are related as combination and subcombination. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the subcombination requires cleavage of a cap structure, which is not required for the basic method of synthesizing a

cDNA molecule. The subcombination has separate utility such as producing full length cDNAs which cleave the cap structure of hybrid mRNA/cDNA. .

3. Because these inventions are distinct for the reasons given above and the search required for Group I is not required for Group II, restriction for examination purposes as indicated is proper.

4. During a telephone conversation with Mr. Robert Esmond on 2/20/2001 a provisional election was made without traverse to prosecute the invention of Group I, claims 33-63. Affirmation of this election must be made by applicant in replying to this Office action. Claims 64-104 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

5. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 102

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

7. Claims 33-39 are rejected under 35 U.S.C. 102(b) as being anticipated by Sloma.

Claim 33 is drawn to a method for synthesizing one or more cDNA molecules or population of cDNA molecules comprising: mixing at least one mRNA template, poly A RNA template or population of such templates with at least one polypeptide having reverse transcriptase activitity; under conditions that inhibit, prevent, reduce, or substantially reduce internal priming. Claim 34 is drawn to the polypeptide being a reverse transcriptase which is selected from the group consisitng of M-MLV RT, RSV RT, AMV RT, MAV RT, and HIV RT, and derivatives and fragments thereof. Claim 35 is drawn to the reverse transcriptase having reduced RNase H activity. Claim 36 is drawn to the primers hybridizing at temperatures that inhibit, prevent, reduce, or substantially reduce internal priming. Claim 37 states that those temperatures are between 10 and 90 degrees C. Claim 38 states that those temperatures are between 20 and 75 degrees C. Claim 39 states that those temperatures are between 45 and 65 degrees C.

Sloma teaches "Synthesis of cDNA employs avian myeloblastosis virus reverse transcriptase. This enzyme catalyzes the synthesis of a single strand of DNA from deoxynucleoside triphosphates on the mRNA template. The poly r(A) tail of mRNA permits oligo (dT) ...to be used as a primer for cDNA synthesis...cDNA synthesis is generally conducted by combining the mRNA, the dNTPs, the oligo (dT) and the reverse transcriptase in a properly buffered solution....This solution is incubated at an elevated temperature of about 40-50 degrees C, for a time sufficient to allow formation of the cDNA copy...(Col. 4, lines 16-37). Therefore, Sloma teaches synthesis of a cDNA molecule, in the presence of an RT such as AMV, which is known to not possess RNase H properties, at an elevated temperature.

Sloma therefore teach all of the limitations of claims 33-39.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 40-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sloma as applied to claims 33-39 above, and further in view of Copeland et al.

Claims 40-42 depend form claim 33, but recite the further limitation that the amount of primer to template ratio is between 15:1 and 1:15, between 10:1 and 1:10, and between 5:1 and 1:5, respectively.

Sloma does not teach primer: template ratios.

Copeland et al. teach that the primer: template ratio is in a ratio of 1:1 in regards to the synthesis of DNA. (Col. 21-22, lines 65-4).

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the method of Sloma with that of Copeland. This is because it was well known in the art at the time of the invention that a variety of template: primer ratios were useable in different circumstances, depending upon the needs of that given reaction. It was also well known that lowering the primer: template ratio would have caused synthesis to proceed at a slower rate, which would have been beneficial in many applications such as cDNA synthesis. It would not have been an undue

experimentation on the part of the practitioner to vary the primer: template ratio until the maximum amount of cDNA product, at the longest length possible, was obtained.

10. Claims 43-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sloma as applied to claims 33-39 above, and further in view of Ranu.

The claims are drawn to the method of claim 33, with the further limitation that a primer is used which has high specificity, and is from a length of 20-100 bases, 20-75 bases, 20-50 bases, and 25-35 bases, respectively.

Sloma does not teach the length of the primers used.

Ranu teaches the use of a 50-mer primer as the antisense oligonucleotide in the synthesis of cDNA from mRNA. (Col. 15, lines 40-45).

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute the primer of Sloma with that of the 50-mer of Ranu, or of any other reasonable size for that matter. This is because it was well known in the art at the time of the invention that primers of many different lengths were readily useable to prime the synthesis of mRNA. Furthermore, it was also well known that the longer the primer, the higher the specificity of the priming. Therefore, one of ordinary skill in the art would have been motivated to use a long primer in the synthesis of cDNA. This is because it would have conferred a higher degree of accuracy in the product, allowing for a longer length product if that primer were directed toward the poly A tail.

Summary

Claims 33-46 are rejected. Claims 47-63 are free of the prior art and are considered allowable. These claims are free of the prior art because they teach an

inhibitor of the polypeptide having reverse transcriptase activity during the synthesis of a cDNA molecule from an mRNA template.

Response to Arguments

11. Applicant's arguments filed 1/20/01 have been fully considered but they are not persuasive in regards to the 102(b) and 103(a) rejections over claims 33-46. In regards to the arguments over the rejection of claims 1-6, 15-16, and 21-30 (now equivalent to claims 33-39), Applicant asserts that the rejection is improper because "Sloma uses this elevated temperature during the DNA synthesis reaction...and not during the annealing phase of the reaction." However, the claim does not specify at what point the temperature is elevated. Applicant also argues that "Sloma does not teach any methods for optimizing the percent yield of double stranded cDNA produced..." However, it is pointed out the claims do not teach optimizing the percent yield of double stranded cDNA produced. In regards to the 103(a) rejection of Sloma in view of Copeland, pertaining to claims 40-42, Applicant states that neither reference teach or suggest the use of a low primer to template ratio in preparing cDNA. However, Copeland teach a ratio of 1:1, which falls in the range disclosed in the claims. In regards to the 103(a) rejection of claims 43-46, Sloma in view of Ranu, Applicant states that Ranu does not teach or suggest a method of using a long primer in cDNA synthesis. However, Ranu does teach the use of a primer in the same range as that disclosed in the claims. Furthermore, it would have been obvious to one of ordinary skill in the art that primer length is variable and a wide range of sizes are known to be effective in amplifying the target nucleic acid.

Conclusion

12. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janell Taylor Cleveland, whose telephone number is (703) 305-0273.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (703) 308-1152.

Any inquiries of a general nature relating to this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed to Group 1634 via the PTO Fax Center using (703) 305-3014 or 305-4227. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989.)

Janell Taylor Cleveland

February 21, 2001

W. Gary Jones
Supervisory Patent Examiner
Technology Center 1600